

## REMARKS

Attached hereto is a marked-up version of the changes made to the specification by the above amendment. The attached page is captioned **“Version with markings to show changes made.”**

The amendment to claim 15 does not alter the scope of the claims but merely recites a feature of “fast breaking” liposomes already present in the claims via claim 15 as originally presented. Support for the amendment is provided at least on page 9 (top half) and page 24 (last paragraph) of the specification as originally filed. The amendment is made for reasons relating to business considerations and commercial embodiments of the invention rather than issues of patentability. No new matter has been added and entry of the amendment is respectfully requested.

Before addressing the Office Action in detail, Applicants respectfully point out that the present invention is directed to liposomal formulations of porphyrin macrocycle photosensitizers that are “fast breaking” such that they quickly deliver the photosensitizers into the lipoprotein compartment of blood. As demonstrated in Table IV (see Example III, pages 24-25), the liposomes of the present invention delivers at least 90% of the associated photosensitizers to lipoproteins by one hour after contact.

### ***Rejection under obviousness type double patenting***

Claims 15-32 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of USP 6,074,666.

Applicants thank the Examiner for indicating that this rejection will be held in abeyance until the claims are found to be otherwise allowable.

***Rejection under 35 U.S.C. § 102(e)***

Claims 15-20 and 30-32 have been rejected under 35 U.S.C. § 102(e) over Madden (USP 5,389,378). Applicants have carefully reviewed the reference and the statement of the rejection and respectfully traverse because no *prima facie* case of anticipation has been presented.

A review of Madden shows that none of the terms “fast breaking”, “bloodstream”, “lipoprotein”, or “blood” are used in the patent. This is because there is simply no disclosure by Madden of any liposomal formulation capable of quickly delivering a porphyrin macrocycle to lipoproteins of the bloodstream.

Moreover, nothing in Madden teaches or indicates that any of the disclosed liposomal formulations are capable of delivering 90% of porphyrin macrocycle photosensitizers to lipoproteins by as little as one hour. As such, Madden fails to disclose all elements of the claimed invention and thus fails to anticipate the claims. Applicants respectfully request this rejection be withdrawn.

***Rejection under 35 U.S.C. § 103(a)***

Claims 15-20 and 25-32 have been rejected under 35 U.S.C. § 103(a) over Thompson et al. (USP 5,277,913) or Kappas et al. (USP 5,010,073) individually in view of Crowe et al. (USP 4,857,319). Applicants have carefully reviewed the references and the statement of the rejection and respectfully traverse because no *prima facie* case of obviousness has been presented.

Similar to the situation with Madden as discussed above, none of the three cited references relied upon in the instant rejection utilize the terms “fast breaking”, “bloodstream”, “lipoprotein”, or “blood”. This is because none of the references disclose or suggest any liposomal formulation capable of quickly delivering a porphyrin macrocycle to lipoproteins of the bloodstream. There is simply no teaching or suggestion in the cited references, or combinations thereof, that would lead to a liposomal formulation capable of delivering 90% of porphyrin macrocycle photosensitizers to lipoproteins by as little as one hour.

Additionally, none of the cited references disclose the particular photosensitizer is that recited in claim 25; the particular ratios of liposomal components recited in claims 26-27; or the inclusion of antioxidants as recited in claims 28-29. Thus the subject matter of claims 25-29 have not been taught or suggested, and no basis for asserting these claims as obvious in light of the cited references has been presented (see MPEP 2143.03 and the case law cited therein).

The statement of the instant rejection asserts that both Thompson et al. and Kappas et al. teach “liposomal porphyrins and photodynamic therapy” but not the presence of sugars, which is taught by Crowe et al.

As noted above, however, the references also fail to teach or suggest “fast breaking” liposomal formulations as encompassed by the instant claims. In the absence of such teachings and suggestions, Applicants respectfully submit that no *prima facie* case of obviousness is present regardless of what the cited references do teach or suggest. This position is even more applicable to claims 25-29 given the presence of additional claim elements not found or suggested by the cited references.

Because the cited references, individually or in any combination, fail to teach or suggest the invention of claims 15-20 and 25-32, no *prima facie* case of obviousness has been presented. Applicants respectfully request that the instant rejection be withdrawn.

Claims 15-32 have been rejected under 35 U.S.C. § 103(a) over Madden (USP 5,389,378) or Thompson et al. (USP 5,277,913) or Kappas et al. (USP 5,010,073) individually in view of Crowe et al. (USP 4,857,319). Applicants have carefully reviewed the references and the statement of the rejection and respectfully traverse because no *prima facie* case of obviousness has been presented.

As an initial matter, and to the extent that the rejection of claims 15-20 and 25-32 over Thompson et al. or Kappas et al. in view of Crowe et al. has been addressed above, Applicants direct attention to the above.

The statement of the instant rejection asserts that none of Madden, Thompson et al., or Kappas et al. teach all of the porphyrin derivatives as recited in the instantly rejected claims, but that it would have been obvious to use “art known porphyrin derivatives in the liposomes of Madden, Thompson et al., or Kappas et al. with the expectation of obtaining similar results”.

Before addressing the instant rejection in detail, Applicants note that once again, elements present in claims 26-29 are not taught or suggested by any of the cited references. These claim elements do not relate to “art known porphyrin derivatives” and so the instant rejection fails to provide any basis for asserting that these claims are obvious over the cited references.

As for claims 15-25 and 30-32, and as discussed repeatedly above, Applicants begin by pointing out that none of the cited references disclose or suggest any liposomal formulation

capable of quickly delivering a porphyrin macrocycle to lipoproteins of the bloodstream. There is simply no teaching or suggestion in the cited references, or combinations thereof, that would lead to a liposomal formulation capable of delivering 90% of porphyrin macrocycle photosensitizers to lipoproteins by as little as one hour. In the absence of such teachings and suggestions, Applicants respectfully submit that no *prima facie* case of obviousness is present.

Moreover, and with respect to the position put forth by the instant rejection that use of any art known porphyrin derivative would be obvious, Applicants respectfully direct attention to the well established principle that the mere *fact that references can be combined or modified is not sufficient to establish a prima facie obviousness* (see MPEP 2143.01 and the case law decisions cited therein). The Federal Circuit has clearly set forth the standard that motivation to combine references must be present and requires a desirable combination of references rather than a combination of what is feasible. *See Winner Int'l Royalty Corp. v. Ching-Rong Wang*, 53 USPQ2d 1580, 1587 (Fed. Cir. 1990). "Although a reference need not expressly teach that the disclosure contained therein should be combined with another, the showing of combinability, in whatever form, must nevertheless be 'clear and particular.'" *Id.* at 1586-87 (quoting *In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted).

The instant rejection, however, provides no showing of why the ordinary artisan would find it desirable to use any known porphyrin derivative as part of a liposomal formulation. Because of this deficiency, the core of the instant rejection fails to be adequately supported by motivation necessary to present a *prima facie* case of obviousness.

In light of the deficiencies discussed above, the cited references, individually or in any combination, fail to teach or suggest the invention of claims 15-32. Applicants thus respectfully request that the instant rejection be withdrawn.

### Conclusion

In light of the above discussion, Applicants respectfully submit that the claims are allowable, and passage of the application to issue is urged. The Examiner is welcome to contact the undersigned to resolve any residual issues, such as the submission of a terminal disclaimer, or if further discussions may be thought useful.

In the event that the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 273012008102. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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## Version with markings to show changes made.

Kindly amend the claims as follows:

15. (amended)        A liposomal formulation comprising liposomes that comprise a porphyrin macrocycle photosensitizer and one or more sugars  
                         wherein said liposomes are fast breaking and rapidly release the photosensitizer into the bloodstream to associate with lipoproteins upon *in vivo* administration.